

Response to Office Action Mailed November 22, 2004

A. Claims in the Case

Claims 309, 311-315, 317-321, and 323-340 are rejected. Claim 316 was objected to as being dependent upon a rejected base claim. Claims 309, 311-321, and 323-340 are pending. Claim 309 has been amended.

B. The Claims Are Not Anticipated by Alberte Pursuant To 35 U.S.C. § 102(e)

The Examiner rejected claims 309, 311, 313-315, 317-321, 323, 325, 329, 330, 333, 335, and 337-339 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,692,696 to Alberte et al. (hereinafter "Alberte"). Applicant respectfully disagrees that the claims are unpatentable over Alberte.

The standard for "anticipation" is one of fairly strict identity. To anticipate a claim of a patent, a single prior source must contain all the claimed essential elements. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 U.S.P.Q.81, 91 (Fed.Cir. 1986); *In re Donahue*, 766 F.2d 531, 226 U.S.P.Q. 619, 621 (Fed.Cir. 1985).

The Office Action stated:

Alberte discloses a system comprising a body, a light source disposed within the body (#36), a cartridge (#28), wherein the cartridge is removable and positionable within the body (Column 21, lines 50-62), wherein the cartridge comprises a body (#30) and a sensor array (#12, FIG. 7) wherein the array comprises a supporting member and at least one cavity within the supporting member (stage #32), particles positioned in the cavity (e.g. binding agent, cells or GPCR). (Office Action, page 3)

Amended claim 309 includes a combination of features including, but not limited to, the features of “a particle, wherein the particle is positioned in the cavity, and wherein the particle is configured to produce a signal when the particle interacts with an analyte during use, and wherein the cavity is configured such that a particle is substantially contained within the cavity during use.”

Support for the amendments to Applicant’s claims can be found in Applicant’s specification, which states:

The supporting member may include a plurality of cavities. The cavities may be formed such that at least one particle is substantially contained within the cavity.
(Specification, page 11, lines 9-10)

Applicant’s Specification further states:

The sensor array, in some embodiments, is formed of a supporting member which is configured to hold a variety of chemically sensitive particles (herein referred to as “particles”) in an ordered array. The particles are, in some embodiments, elements which will create a detectable signal in the presence of an analyte. The particles may produce optical (e.g., absorbance or reflectance) or fluorescence/phosphorescent signals upon exposure to an analyte. Examples of particles include, but are not limited to functionalized polymeric beads, agarous beads, dextrose beads, polyacrylamide beads, control pore glass beads, metal oxides particles (e.g., silicon dioxide (SiO₂) or aluminum oxides (Al₂O₃)), polymer thin films, metal quantum particles (e.g., silver, gold, platinum, etc.), and semiconductor quantum particles (e.g., Si, Ge, GaAs, etc.). (Applicant’s Specification, page 7, line 24 - page 8, line 3);

The particles may include a receptor molecule coupled to a polymeric bead. The receptors, in some embodiments, are chosen for interacting with analytes. This interaction may take the form of a binding/association of the receptors with the analytes. (Applicant’s Specification, page 8, lines 17-20); and

The receptor molecules may be naturally occurring or synthetic receptors formed by rational design or combinatorial methods. Some examples of natural receptors include, but are not limited to, DNA, RNA, proteins, enzymes, oligopeptides,

antigens, and antibodies. Either natural or synthetic receptors may be chosen for their ability to bind to the analyte molecules in a specific manner. In one embodiment, a naturally occurring or synthetic receptor is bound to a polymeric bead in order to create the particle. The particle, in some embodiments, is capable of both binding the analyte(s) of interest and creating a detectable signal. (Applicant's Specification, page 9, lines 14-22).

Alberte does not appear to teach particles. Alberte appears to teach GPCRs on a cell surface. Alberte states:

A "G-Protein Coupled Receptor" (GPCR) is defined to be any cell surface transmembrane protein that when activated by the binding of a chemical ligand or specific substance, in turn activates a heterimeric guanine nucleotide-binding protein...In living cells, GPCRs are localized within cell membranes and operate to communicate chemical signals...from the extracellular environment to the inside of the cell. (Alberte, column 12, line 60 - column 13, line 1); and

A GPCR is considered to be useful in those aspects of the present invention which employ cell-based sensors. In particular, the cells are transformed and heterologously express a GPCR that is coupled to an endogenous calcium channel. The term "heterologous expression" means transcription and translation of nucleotide sequences which are not native to the cell but which have been incorporated into the cell's chromosomal or extra-chromosomal expression system genetic engineering techniques known in the art. (Alberte, column 13, lines 41-49).

Alberte teaches modifying cells so that GPCRs on the cells will select a desired ligand. Alberte does not appear to teach or suggest using a particle in a cavity.

Alberte also does not appear to teach or suggest positioning a particle within a cavity where the cavity is configured to substantially contain the particle within the cavity. Alberte states:

GPCRs are oriented 78 and immobilized and stabilized 80 in functional form for purposes of making the sensing element 12 of the invention. (Alberte, column 18, lines 23-25);

The CPCR-containing cells 14, supported by hydrogel 16 which has been anchored to an optically-opaque, light absorptive stage 32 are disposed preferably but not necessarily as a monolayer which is protected from mechanical distress or excess dehydration by a semipermeable membrane. (Alberte, column 22, lines 18-23); and

cells 14 may be retained in a cartridge by means of a binding agent 16 that is biologically compatible with the cells and provides nutrition for the cells. A preferred class of binding agents is hydrogels. (Alberte, column 22, lines 37-40).

Alberte appears to teach immobilizing cells, such as in a hydrogel. Alberte does not appear to teach or suggest positioning a particle in a cavity that is configured to substantially contain the particle in the cavity during use. Applicant submits that Alberte does not appear to teach or suggest all the features of the claims. Applicant respectfully requests removal of the rejections to claim 309 and the claims dependent thereon.

The Office Action included a rejection of claim 311 in view of Alberte. Claim 311 includes the feature of “a sample input port, wherein the sample input is positioned on the body, and wherein the sample input port is coupled to the sensor array such that samples introduced into the input port are transferred to the sensor array” in combination with the features of claim 309. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 311 in combination with the features of claim 309.

The Office Action included a rejection of claim 313 in view of Alberte. Claim 313 includes the feature of “a sample input port and a filter, wherein the sample input is positioned on the body, and wherein the sample input port is coupled to the sensor array such that samples introduced into the input port are transferred to the sensor array, and wherein the filter is coupled to the sample input port” in combination with the features of claim 309. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 313 in combination with the features of claim 309.

The Office Action included a rejection of claim 314 in view of *Alberte*. Claim 314 includes the feature of “a fluid cartridge coupled to the body and the sensor array” in combination with the features of claim 309. Applicant’s Specification states:

In one embodiment, all of the necessary fluids required for the chemical/biochemical analyses are contained within the portable sensor array system. The fluids may be stored in one or more cartridges 1050. The cartridges 1050 may be removable from the portable sensor array system. Thus, when a cartridge 1050 is emptied of fluid, the cartridge may be replaced by a new cartridge or removed and refilled with fluid. The cartridges 1050 may also be removed and replaced with cartridges filled with different fluids when the sensor array cartridge is changed. Thus, the fluids may be customized for the specific tests being run. Fluid cartridges may be removable or may be formed as an integral part of the reader. (Applicant’s Specification, page 170, lines 5-12).

Alberte states “[e]xposing means 22 typically include a flow chamber in which the cartridge 28 is mounted for intaking a vapor stream or a liquid stream containing a candidate substance.” (*Alberte*, column 22, line 66 - column 23, line 1). *Alberte* appears to teach a flow chamber that intakes vapor or liquid streams. *Alberte* does not appear to teach or suggest a fluid cartridge. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 314 in combination with the features of claim 309.

The Office Action included a rejection of claim 315 in view of *Alberte*. Claim 315 includes the feature of “an electronic controller disposed in the body and coupled to the sensor array, the light source, and the detector; wherein the electronic controller is configured to control the operation of the sensor array system” in combination with the features of claim 309. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 315 in combination with the features of claim 309.

The Office Action included a rejection of claim 317 in view of Alberte. Claim 317 includes the feature of “a data transfer system” in combination with the features of claim 309. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 317 in combination with the features of claim 309.

The Office Action included a rejection of claim 318 in view of Alberte. Claim 318 includes the feature of “wherein the detector comprises a monochrome detector” in combination with the features of claim 309. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 318 in combination with the features of claim 309.

The Office Action included a rejection of claim 319 in view of Alberte. Claim 319 includes the feature of “wherein the detector comprises a color detector” in combination with the features of claim 309. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 319 in combination with the features of claim 309.

The Office Action included a rejection of claim 320 in view of Alberte. Claim 320 includes the feature of “wherein the light source comprises at least one light-emitting diode” in combination with the features of claim 309. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 320 in combination with the features of claim 309.

The Office Action included a rejection of claim 321 in view of Alberte. Claim 321 includes the feature of “wherein the light source comprises a light emitting diode” in combination with the features of claim 309. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 321 in combination with the features of claim 309.

The Office Action included a rejection of claim 323 in view of Alberte. Claim 323 includes the feature of “a fluid delivery system coupled to the supporting member” in

combination with the features of claim 309. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 323 in combination with the features of claim 309.

The Office Action included a rejection of claim 325 in view of Alberte. Claim 325 includes the feature of “wherein the particle comprises a receptor molecule coupled to a polymeric resin” in combination with the features of claim 309. Alberte appears to teach immobilizing a cell in a hydrogel. (Alberte, column 18, lines 23-25; column 22, lines 18-23, 37-40) Alberte does not appear to teach a particle positioned in a cavity. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 325 in combination with the features of claim 309.

The Office Action included a rejection of claim 329 in view of Alberte. Claim 329 includes the feature of “wherein the particle further comprises a first indicator and a second indicator, wherein the first and second indicators are configured to be coupled to a receptor, wherein the interaction of the receptor with the analyte causes the first and second indicators to interact such that the signal is produced” in combination with the features of claim 309. Applicant’s Specification states:

In one embodiment, a detectable signal may be caused by the altering of the physical properties of an indicator ligand bound to the receptor or the polymeric resin. In one embodiment, two different indicators are attached to a receptor or the polymeric resin. When an analyte is captured by the receptor, the physical distance between the two indicators may be altered such that a change in the spectroscopic properties of the indicators is produced. A variety of fluorescent and phosphorescent indicators may be used for this sensing scheme. This process, known as Forster energy transfer, is extremely sensitive to small changes in the distance between the indicator molecules. (Applicant’s Specification, page 35, line 29 – page 36, line 6).

Alberte states:

The transformed yeast cells are incubated in a Ca⁺⁺ binding fluorophore permeable to the transformed cell membrane. In operation, GPCR binding of a

ligand of interest opens up a calcium channel, allowing an influx of free Ca^{++} into the cell, which is rapidly bound by the fluorophore which immediately changes the fluorescence properties of the cell. (Alberte, column 20, lines 55-61).

Alberte appears to teach a signal produced by an influx of Ca^{++} . Alberte does not appear to teach a first and a second indicator coupled to a receptor of a particle. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 329 in combination with the features of claim 309.

The Office Action included a rejection of claim 330 in view of Alberte. Claim 330 includes the feature of “wherein the particles further comprises an indicator, wherein the indicator is associated with a receptor such that in the presence of the analyte the indicator is displaced from the receptor to produce the signal” in combination with the features of claim 309. Alberte appears to teach GPCRs on a cell surface. (Alberte, column 12, line 60 - column 13, line 1; column 13, lines 41-49). Alberte does not appear to teach particles. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 330 in combination with the features of claim 309.

The Office Action included a rejection of claim 333 in view of Alberte. Claim 333 includes the feature of “wherein the supporting member further comprises a barrier layer positioned over the cavity, wherein the barrier layer is configured to inhibit dislodgment of the particle during use” in combination with the features of claim 309. Alberte appears to teach GPCRs on a cell surface. (Alberte, column 12, line 60 - column 13, line 1; column 13, lines 41-49). Alberte does not appear to teach particles. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 333 in combination with the features of claim 309.

The Office Action included a rejection of claim 335 in view of Alberte. Claim 335 includes the feature of “wherein the supporting member further comprises a barrier layer positioned over the cavity, wherein the barrier layer is configured to inhibit dislodgment of the particle during use” in combination with the features of claim 309. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 335 in combination with the features of claim 309.

The Office Action included a rejection of claim 337 in view of Alberte. Claim 337 includes the feature of “wherein the cavity is configured such that the fluid entering the cavity passes through the cavity during use” in combination with the features of claim 309. Alberte appears to teach fluid (arrows in FIGS.) flowing over the cartridge body (30) during use. (FIGS. 1-3). Alberte does not appear to teach or suggest a cavity configured such that fluid entering the cavity passes through the cavity during use. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 337 in combination with the features of claim 309.

The Office Action included a rejection of claim 338 in view of Alberte. Claim 338 includes the feature of “a pump coupled to the supporting member, wherein the pump is configured to direct the fluid towards the cavity” in combination with the features of claim 309. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 338 in combination with the features of claim 309.

The Office Action included a rejection of claim 339 in view of Alberte. Claim 339 includes the feature of “wherein a channel is formed in the supporting member, wherein the channel couples a pump to the cavity such that the fluid flows through the channel to the cavity during use” in combination with the features of claim 309. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 339 in combination with the features of claim 309.

C. The Claims Are Not Obvious Over Alberte In View Of Stabile Pursuant To 35 U.S.C. § 103(a)

The Examiner rejected claims 324, 326-328, 331, 332, 334, 336, and 340 under 35 U.S.C. § 103(a) as being obvious over Alberte in view of U.S. Patent No. 5,872,623 to Stabile et al. (hereinafter “Stabile”). Applicant respectfully disagrees that the claims are unpatentable over Alberte in view of Stabile.

The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680 (Fed. Cir. 1990); MPEP 2143.01. A statement that modifications of the prior art to meet the claimed invention would have been “well within the ordinary skill of the art at the time the claimed invention was made” because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a prima facie case of obviousness without some objective reason to combine the teachings of the references. *Ex parte Levengood*, 28 U.S.P.Q.2d 1300 (Bd. Pat. App. & Inter. 1993); *see also In re Kotzab*, 217 F.3d 1365, 1371 (Fed. Cir. 2000); MPEP 2143.01.

The Office Action states:

Alberte discloses a system comprising a body, a light source disposed within the body (#36), a cartridge (#28), wherein the cartridge is removable and positionable within the body (Column 21, lines 50-62), wherein the cartridge comprises a body (#30) and a sensor array (#12, Fig. 7) wherein the array comprises a supporting member and at least one cavity within the supporting member (stage #32), a particles positioned in the cavity...Alberte does not teach the detector comprises a charge-coupled device; a plurality of particles in a plurality of cavities, wherein the particles ranges from about 0.05 microns to about 500 microns wherein the volume of the particle changes when contacted; wherein the supporting member comprises silicon; a transparent barrier over the cavity to provide a channel; or a

dry film photoresist...However these elements were well known in the art and routinely practiced as taught by Stabile who teach a similar device comprising a substrate having cavities with particles therein. (Office Action, page 6).

Applicant submits that Alberte and Stabile do not teach similar devices and that there is no motivation to combine the references. Alberte appears to teach GPCRs on a cell surface. (Alberte, column 12, line 60 - column 13, line 1; column 13, lines 41-49). Alberte also appears to teach immobilizing a cell in a hydrogel. (Alberte, column 18, lines 23-25; column 22, lines 18-23, 37-40) Alberte does not appear to teach particles or a particle positioned in a cavity. Alberte also teaches “multiple sensing elements in multiple demountable cartridges that include GPCRs which are preferentially responsive to the specific substance.” (Alberte, column 27, lines 46-48).

Stabile states:

The reaction cells or detection sites are preferably found on a planar substrate 105 that is separable from the portion of the liquid distribution system containing reservoirs and pumps. The separable planar substrate 105 docks with the liquid distribution system, typically with a gasket material (that has openings at appropriate locations) interposed between the two, so that the cells are aligned underneath the appropriate outlet for delivering liquid from the liquid distribution system. (Stabile column 14, lines 1-9)

Stabile appears to teach a substrate that is removable from a liquid distribution system. Stabile does not appear to teach or suggest a body including a light source and detector and a sensor array within a cartridge that is removable from the body. Applicant submits that there is no motivation to combine the demountable cartridges that include cells immobilized in hydrogel of Alberte with the system of Stabile.

In addition, Applicant submits that the references do not appear to teach all the features of the claims. The Office Action states “Alberte discloses a system comprising at least one cavity

within the supporting member (stage #32), a particles positioned in the cavity.” (Office Action, page 6).

Claims 324, 326-328, 331, 332, 334, 336, and 340 depend on claim 309 which includes a combination of features including, but not limited to, the features of “a particle, wherein the particle is positioned in the cavity, and wherein the particle is configured to produce a signal when the particle interacts with an analyte during use, and wherein the cavity is configured such that a particle is substantially contained within the cavity during use.” For at least the reasons previously mentioned Applicant submits that the cited art does not appear to teach particles or a cavity configured to substantially contain a particle within the cavity during use. Applicant respectfully requests removal of the rejection to the claims.

If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988). Applicant submits, however, that claims 324, 326-328, 331, 332, 334, 336, and 340 dependent on claim 309 are separately patentable.

The Office Action included a rejection of claim 324 in view of Alberte. Claim 324 includes the feature of “wherein the detector comprises a charge-coupled device” in combination with the features of claim 309. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 324 in combination with the features of claim 309.

The Office Action included a rejection of claim 326 in view of Alberte. Claim 326 includes the feature of “wherein the system comprises a plurality of particles positioned within a plurality of cavities, and wherein the system is configured to substantially simultaneously detect a plurality of analytes in the fluid” in combination with the features of claim 309. Applicant

respectfully submits that the cited art does not teach or suggest the features in claim 326 in combination with the features of claim 309.

The Office Action included a rejection of claim 327 in view of Alberte. Claim 327 includes the feature of “wherein the particle ranges from about 0.05 micron to about 500 microns” in combination with the features of claim 309. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 327 in combination with the features of claim 309.

The Office Action included a rejection of claim 328 in view of Alberte. Claim 328 includes the feature of “wherein a volume of the particle changes when contacted with the fluid” in combination with the features of claim 309. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 328 in combination with the features of claim 309.

The Office Action included a rejection of claim 331 in view of Alberte. Claim 331 includes the feature of “wherein the supporting member comprises silicon” in combination with the features of claim 309. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 331 in combination with the features of claim 309.

The Office Action included a rejection of claim 332 in view of Alberte. Claim 332 includes the feature of “wherein the supporting member further comprises channels in the supporting member, wherein the channels are configured to allow the fluid to flow through the channels into and away from the cavity” in combination with the features of claim 309. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 332 in combination with the features of claim 309.

The Office Action included a rejection of claim 334 in view of Alberte. Claim 334 includes the feature of “wherein the supporting member further comprises a barrier layer positioned over the cavity, wherein the barrier layer is configured to inhibit dislodgment of the particle during use, and wherein the barrier layer comprises a substantially transparent cover plate positioned over the cavity, and wherein the barrier layer is positioned such that a channel is formed between an upper surface of the supporting member and the barrier layer, and wherein the fluid passes through the channel during use” in combination with the features of claim 309. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 334 in combination with the features of claim 309.

The Office Action included a rejection of claim 336 in view of Alberte. Claim 336 includes the feature of “wherein the supporting member comprises a dry film photoresist material” in combination with the features of claim 309. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 336 in combination with the features of claim 309.

The Office Action included a rejection of claim 340 in view of Alberte. Claim 340 includes the feature of “a vacuum apparatus coupled to the sensor array, wherein the vacuum apparatus is configured to pull the fluid through the cavity during use” in combination with the features of claim 309. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 340 in combination with the features of claim 309.

D. The Claims Are Not Obvious Over Alberte In View Of Wilding Pursuant To 35 U.S.C. § 103(a)

The Examiner rejected claim 312 under 35 U.S.C. § 103(a) as being obvious over Alberte in view of U.S. Patent No. 5,587,128 to Wilding et al. (hereinafter “Wilding”). Applicant respectfully disagrees that the claims are unpatentable over Alberte in view of Wilding.

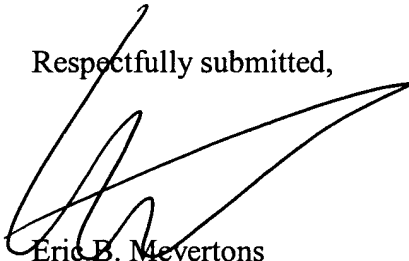
The Office Action included a rejection of claim 312 in view of Alberte. Claim 312 includes the feature of “further comprising a sample input port, wherein the sample input is positioned on the body, and wherein the sample input port is coupled to the sensor array such that samples introduced into the input port are transferred to the sensor array, and wherein the sample input port is configured to receive a syringe” in combination with the features of claim 309. Applicant respectfully submits that the cited art does not teach or suggest the features in claim 312 in combination with the features of claim 309.

E. Summary

Applicant submits that all claims are in condition for allowance. Favorable reconsideration is respectfully requested.

Applicant respectfully requests a one-month extension of time. If any additional extension of time is required, Applicant hereby requests the appropriate extension of time. A Fee Authorization is enclosed for the one-month extension of time fee. If any fees have been inadvertently omitted or if any fees are required, please charge those fees to Meyertons, Hood, Kivlin, Kowert & Goetzel, P.C. Deposit Account Number 50-1505/5936-00529/EBM.

Respectfully submitted,



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